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INTESTINAL OBSTRUCTION—PART II

N. KALANT, 4T7

In the second half of this paper I shall discuss the diagnosis and treatment of intestinal obstruction, especially with regard to the relation of these, to the physiological principles discussed previously.

Diagnosis

There is usually little difficulty in determining that intestinal obstruction exists. The patient complains of one or more of abdominal pain, vomiting, enlarging abdomen, and constipation.

The pain is initially crampy, the duration of cramps depending on the location of the obstructing mechanism; if in the small bowel they are 3-10 minutes long; if in the colon they are 15-30 minutes long. Later as transudate reaches the peritoneal surface of the gut, a steady pain is experienced as well as the cramps.

Vomiting varies in intensity, being abundant and continuous in small bowel obstructions. It is not fecal until quite late—perhaps too late. Theoretically, vomiting in colonic obstruction should be slight and of a reflex nature, since regurgitation of contents into the ileum is prevented by the ileo-cecal valve. In fact, it does occur to a considerable degree, in about 30% of such cases, because of incompetency of this valve.

Distention is determined by the degree, as well as the site, of the obstruction. In the small gut, it is slight because vomiting prevents the accumulation of excess fluids. In the colon, for the same reason that vomiting tends to be a minor factor, distention is a major factor. The great colonic distention results, not infrequently, in perforation of the cecum.

Constipation may be complete or incomplete, varying with the degree of the obstruction. This symptom is obviously of much greater significance in diagnosing a chronic lesion than an acute one.

The clinical signs are those one would expect to find.

1. Distention, increasing with the duration of the symptoms.

2. Tenderness and rigidity, present in strangulated lesions and in late simple cases where transudate has reached the serosa.

3. Palpable mass, present in some cases, depending on the cause of the obstruction.

4. Visible peristalsis, in subacute cases.

5. Dehydration, especially in late cases of high obstruction.

6. Shock, if there is strangulation of the bowel.

7. Peristaltic noises. These are changed, becoming high pitched and tinkling while peristalsis is active, or greatly diminished or absent if peristalsis ceases, as in paralytic ileus. These changes are evident within two hours of the onset of the obstruction. Wangenstien lays great stress upon the occurrence of these borborygmi, simultaneous with the peak of the colicky pains, and he dogmatically states that without this sign intestinal obstruction does not exist. Some patients, however, do not know this rule; a case report in a recent journal tells of a girl with intestinal obstruction, whose signs and symptoms did not meet Wangenstien's criterion for obstruction.

The laboratory findings are also straightforward.

1. The urine is scant because of vomiting and increased secretion of intestional fluid.

2. The white cell count is usually normal. A rise usually indicates strangulation.

3. The blood chlorides fall and the CO_2 combining power rises in late high obstruction, varying with the degree of vomiting.

4. The blood N.P.N. level rises, frequently in small bowel lesions, rarely in colonic. Falconer has said that the N.P.N. is the best index of the patient's condition, and that it varies directly with the degree of obstruction. Most others regard the rise in N.P.N. as just another indication of haemoconcentration, and toxic destruction of protein.

5. Rapid blood loss with low haemoglobin and low haematocrit values occur in strangulation.

6. X-ray. This is a particularly valuable aid in diagnosis, giving positive evidence of obstruction within four hours of the onset. A scout film of the abdomen should be taken as soon as possible if the condition is suspected. Interpretations of the plate are based on the answers to these three questions:

(a) Is there gas in the G. I. Tract?
(b) Is it in the colon, small intestine or both?
(c) If in both, what are the relative amounts in each?

Briefly, the significance of these questions is as follows: since distention in obstruction is, in large measure, due to gas, the absence of excess gas in the G. I. Tract indicates the absence of obstruction. If gas is present in the small bowel only, then there is an obstructing mechanism in the large bowel, which has been transformed by a competent ileo-cecal valve, into a closed loop. Equal distention of large and small intestines implies an adynamic ileus. Marked distention of the small gut with some gas in the large suggests an incomplete obstruction of the small gut. The ladder pattern of coils of intestine is a relatively late finding. If some of the gas in the abdomen is found not to rise to the uppermost side when the patient is placed horizontally, it must be contained in a loop closed at both ends. Consequently, such a finding indicates a closed loop obstruction. A barium enema may be of value, but a barium meal is emphatically contra-indicated.

Though we are often reminded of the danger of making a diagnosis on the basis of X-rays, it is significant that Zeitlin and Mazel claimed almost 100% accuracy in diagnosis by scout films, sometimes in the absence of clinical signs.

With the information gained by history, physical examination and laboratory tests, we must try to determine not only the presence and site of obstruction, but also the cause and type of lesion, for these things will aid in deciding the proper management of the patient. Our diagnosis should, when possible, answer these questions as proposed by Wangenstein: Is there obstruction? Where is it? Is it complete? Is it strangulated or simple? What is the cause?

With respect to the last question, we must take the history into account. The age of the patient is often of great help. Congenital lesions and intussusception would be expected in children; carcinoma and hernia in adults; a history of previous operation suggests adhesions.

The differential diagnosis must rule out simple enterocolitis and food poisoning as well as many more serious intraperitoeal lesions as acute cholecystitis, salpigitis, pancreatitis, nephrolithiasis, etc. It is important to realize that many of these other conditions may secondarily cause intestinal obstruction by mechanical means, or by producing ileus. It must also be remembered that a strangulating lesion of the intestine may not produce obstruction-viz. vascular lesions, such as mesenteric thrombosis, embolism and Richter's hernia.

Treatment

It is in the treatment that the greatest difficulty lies, for the mortality of intestinal obstruction always has been very high. Nevertheless, the results of treatment today are much better than 20 years ago and the reason is that surgeons have been applying some of the physiological principles discussed above. If there is loss of electrolytes and fluids, then replace these substances; if there is shock due to haemorrhage into the bowel, then transfuse with blood or plasma; if death results from distention, prevent it by relieving the distention; if peritonitis is due to soiling of the peritoneum with fecal material, then use aseptic operative technique.

The various factors concerned in treatment will now be discussed.

1. Administration of saline.

This practice is of real use only in patients suffering from a loss of water and electrolytes—i.e. patients with a high small bowel obstruction who are vomiting all their gastric and pancreatic juices. Since most cases are of low obstruction, saline has a limited value as a specific treatment. However, it is still important in maintaining general water and salt balance in an operative patient. Since vomited fluid has not the composition of normal saline, administration of normal saline will not rectify the loss; the water and electrolytes must be considered separately. The fluid must provide for normal losses as well as for replacement of that lost by previous vomiting, continued vomiting and by aspiration of intestinal contents.

2. Blood and plasma.

The use of these is of great importance in many patients. There is an obvious indication for blood or blood substitute in cases of strangulating lesions, for here, unless the arterial supply, as well as the venous, is cut off, there may be remarkably large haemorrhage into the gut wall. The circulating blood volume may be reduced by 50% or more, and a replacement of this volume occurs from the extra-cellular body fluid, the haemoglobin correspondingly falls. There is no doubt that shock may occur in acute obstruction even though haemorrhagic infarction is not present; here too, transfusion is useful. Patients with chronic obstruction usually have a low plasma volume because of poor protein absorption from the gut; in such cases, plasma should be given pre-operatively and post-operatively. In late simple obstruction, pooling of fluid in the bowel lumen causes a reduction in the circulating blood volume, which should be corrected by fluid or plasma administration.

3. Oxygen.

As Wangenstien has shown, the gas in the intestinal lumen, in distention, is swallowed air; this implies a high concentration of nitrogen, which in fact forms 70% of the gas. Fine and co-workers decided that a method of relieving this gaseous distention would be to have the blood carry the gas to the lungs where it might be expired. To this end, they devised the scheme of inhaling pure oxygen. This decreases the partial pressure of nitrogen in the blood from its normal of 570 mm. down to a minimum, thus raising the rate of absorption of this gas from the gut. On reaching the lung the nitrogen readily passes into the alveoli where its partial pressure is low. Since the distention is due, in large part, to fluid as well as gas, this procedure can, at best, reduce it only partially. However, if oxygen is used in conjunction with other decompression measures, it is of great value in speeding the process.

4. Adrenal cortical extract.

Laufman and Freed found that injection of transudate from a strangulated loop caused a general increase in capillary permeability and postulated that in

strangulating obstruction, such a substance enters the blood stream and damages the body capillaries, thus leading to a loss of intra-vascular fluid, shock and death. Experimentally they found that injections of cortin, to prevent capillary damage, prolonged life if given in conjunction with loop transudate. Clinical reports have been poor.

5. Antibacterial and antibiotic drugs.

As described in the first half of this paper, the presence of certain sulphonamides in a closed loop of bowel, prevented death in spite of distention, if given at the time of production of the loop. Penicillin given parenterally after production of a strangulated loop, prolonged life for a considerable length of time. The sulphonamides which are most useful are those which are absorbed slowly—Sulphasuccidine, sulphaguanidine, and sulphathalidine. Penicillin is of value since it is effective against Streptococcus fecalis, which, rather than B. coli is the important pathogen in peritonitis. However, it must be given in massive doses to overcome the penicillinase produced by the B. coli. There are several practical applications for these drugs:

(a) They have an obvious and undisputed place in obstruction due to inflammatory conditions, such as diverticulitis.
(b) Given pre-operatively, they can reduce the number of pathogens in the bowel, so reducing the risk of peritonitis following accidental spillage, during operation.
(c) Other factors allowing, they make possible a one stage operation rather than multi-staged procedures.
(d) The promise of greatest help lies in the ability of penicillin to prolong life in the presence of strangulation. This will be mentioned later.

6. Intestinal intubation.

When it was realized that death in simple obstruction was, in large measure, due to distention, the idea was conceived of making a direct, but not operative attack on the distending substances to effect decompression. Wangenstien (1933) applied suction to an inlying duodenal tube, and by this simple, but effective method, made a great advance in the conservative treatment of obstruction. One disadvantage of this method was that it became necessary to drain the whole bowel between the duodenum and the site of the obstruction in order to decompress the region most subject to the effects of pressure viz. the part just proximal to the obstruction. This difficulty was overcome by the introduction, by Miller and Abbott, of a balloon-tipped tube whose end is carried by peristalis down to the site of obstruction, so that this region can be emptied at once.

Intubation can be used in every case of intestinal obstruction. In some early simple bowel obstruction and in many cases of ileus it is the only treatment needed. This does not apply to ileus due to peritonitis, where decompression has little effect. The procedure is of use in all cases going to operation; Suction should be in force before, during, and after operation, with a definite purpose during each period.

Pre-operatively it decreases tension on the gut wall, allows the muscle fibres to contract and thicken, and thus makes the handling of the bowel safer, reducing the danger of perforation. During operation it keeps the stomach empty, preventing aspiration following the reflex vomiting which so often results from traction on the mesentery. Post-operatively it prevents distention due to ileus; it allows feeding per os, a good deal of absorption, and removal of the residue before it reaches the suture line.

Some of the difficulties in using the inlying tube are:

(a) Difficulty in getting it past the pyloris. Many modifications of the Miller-Abbott tube have been suggested to obviate this difficulty. When possible, the tube should be passed with the aid of the fluoroscope.

(b) Overdistention of the balloon leading to its arrest or rupture. This can be overcome by testing before its introduction and determining how much air is required to inflate that particular balloon.

(c) Sore throat and laryngeal oedema. The soreness is never serious and can be relieved by pontocaine. Laryngeal oedema is rare, but may be severe enough to necessitate tracheotomy.

(d) Otitis media may occur in children.

When large quantities of fluid are being withdrawn, the suction apparatus should include a trap bottle to retain the aspirated fluid. This enables a more accurate calculation of fluid replacement needs.

The criteria of successful decompression are: cessation of gas pains, decreasing distention, presence of gas in the colon if it was not there previously, decreasing amounts of aspirated material, and no discomfort on stopping aspiration for an hour or more.

7. Operation.

Operation is the most important single therapeutic procedure in a large majority of cases. In spite of transfusions, penicillin and Miller-Abbott tubes, it remains the only direct attack on the obstructing mechanism. It is essential in most cases, for intubation cannot untwist a volvulus, nor antibiotics dissolve an impacted gall stone.

Of importance with respect to operative success, are the type of operation undertaken, the skill of the surgeon and the duration of the operation. The last two factors, as well as the cause of the obstruction, will determine the type of operation. The various procedures used are either direct attacks to eliminate the obstructing mechanism, or indirect methods of minimizing the effect of obstruction.

Direct Measures.

(a) Division of adhesions; this can be done safely in early cases, but after several days the band tends to fuse with the bowel wall so that there is great danger of perforation if lysis is attempted.

(b) Excision with primary anastomosis. Excision is necessary when part of the bowel wall is not viable, because of impaired blood supply or the effects of

pressure. Primary anastomosis, though still a formidable procedure, has been made safer by the continuous use of the Miller-Abbott tube, and by the use of sulphonamides and penicillin topically about the anastomosis.

(c) Other procedures, such as reduction of a hernia, or intussusception or crushing of a gall stone.

Indirect Measures.

(a) Decompressive enterostomy. This not uncommonly performed on the small intestine, but is also widely used in the colon where suction decompression cannot be achieved. Since most large bowel obstructions are in the descending colon or sigmoid, transverse colostomy is permissible, and is now taking the place of blind cecostomy. It has the advantage of allowing a complete diversion of the fecal stream; according to Dennison's results, it is safer than cecostomy.

(b) and (c) Exteriorization with fistula and entero-anastomosis to by-pass the obstruction. The principle in these is the same. One, however, necessitates establishment of a temporary external fistula, while the other entails a permanent internal fistula. The former permits the observation of the exteriorized segment and so is of value when the viability of this section is in doubt. It can later be returned to the abdomen or excised. Entero-anastomosis is usually used only when other treatment is contra-indicated.

Post-operative treatment carries certain problems, chiefly of prophylaxis. The danger of shock following operation is higher in intestinal obstruction than in other conditions, chiefly because of the patient's condition to start with, and also because of traction of the mesentery at operation. It is because of this danger that pre-operative preparation with saline, blood and plasma as needed, is of such great importance.

The greatest danger to the patient lies in pulmonary accidents, such as atelectasis, aspiration pneumonia and embolism.

Atelectasis is a threat particularly in upper abdominal operations since operative trauma may lead to inhibition of the diaphragm and consequent lack of aeration of the lower lobes. Use of 5% carbon dioxide will stimulate respiration.

Aspiration pneumonia is apt to occur because of operative trauma leading to vomiting. Early and continued use of intubation and suction should reduce this to a minimum.

Pulmonary embolism is a more frequent complication of intestinal obstruction than of many other abdominal conditions. The reason for this is not clear. Theoretically the incidence of spontaneous thrombosis should be lowered since the prothrombin time is raised to about 100 seconds and the prothrombin level decreased to 10 units or less. However, a markedly distended bowel exerts pressure on the iliac veins, conceivably slowing circulation from the lower limbs to such a degree that thrombosis can occur. Such an idea implies that relief of distention, either operatively or non-operatively, would decrease the tendency to thrombosis, so that if clotting did occur it would do so before treatment rather than post-operatively. Since there is no evidence that this is so, we must fall back and repeat that the

reason for the high incidence of phlebothrombosis and pulmonary embolism is not clear. The prevention is the same as in other conditions.

MANAGEMENT OF A CASE.

The patient may be treated conservatively or operatively. Conservative management consists of re-establishing normal salt and water balance, as described, transfusion of blood or plasma if needed, and decompression by suction through a Miller-Abbott tube. Feeding may be done by mouth in some cases, but in others must be done intravenously with glucose and amigen. Operative treatment would include all these (except the last) in pre-operative treatment, to be followed by surgical intervention, and then renewed as post-operative treatment.

Any patient treated conservatively should have a scout film taken every 12 hours, a leucocyte count twice daily and an abdominal examination every 6-8 hours. These will show the progress under treatment and will enable early recognition of a change to strangulating type of obstruction.

There are two schools of thought as to the best management, based on the value attached to conservative treatment. Briefly, the evolution of the trends in treatment is this: with the introduction of Wangenstien suction and the Miller-Abbott tube, there was a sharp fall in mortality from the 40% range to 20%. Suction decompression presented a great step forward, and everyone began to use it. However, as with most new things, it was frequently misused and was allowed to take the place of operation, with fatal results. Thus it was seen to be a mixed blessing, which, if not understood, could do much harm. As a reaction, there was a tendency to avoid conservative treatment and to operate on all cases. Now as conservative treatment is being more soberly assessed there is a trend toward its cautious use.

Wangenstien, one of the foremost proponents of decompression, in each patient attempts to determine whether or not the obstruction is strangulating, basing the differentiation on the presence of tenderness and a rising leucocyte count in strangulation. He gives as absolute indications for operation (a) all strangulating obstructions. (b) all obstructions of the colon with great distention, indicating a closed loop effect; (c) certain types of simple obstruction where surgery is inevitable.

In other cases, he uses conservative treatment for a trial period of about 6 hours. In many cases of early simple obstruction decompression is enough to allow re-establishment of the bowel lumen.

McKittrick (1940) voiced the opinion of many others when he stated that he cannot tell clinically whether strangulation is present or not. He contended that the exceptions to the rule of "tenderness with intestinal colic" are too frequent to allow reliance on that rule. Consequently, he governs his action by the duration of symptoms. Immediate operation is done on all cases seen within 24 hours of the onset of symptoms. Delayed operation or non-operative treatment is carried out in patients seen after 48 hours who show no definite signs of strangulation, and in patients over 60 years of age.

Typifying the present trend, Moses (1946) stressed the importance of not adhering to rules about early operation, but of operating only when the patient is in proper condition for the procedure.

The use of penicillin and sulphas is an added factor to be considered in this discussion. If the experimental results are duplicated clinically, then these drugs will prolong the period of safe conservative therapy, allowing further investigation, more time to improve the patient's general condition, and a better chance to determine the results of intubation. They cannot take the place of surgery, but they can add to conservative therapy. Should operation be undertaken, they can reduce the incidence of peritonitis which accounts for over 60% of deaths.

There has been a marked fall in the mortality rate of intestinal obstruction since the turn of the century, the drop in each era corresponding to the introduction of a new therapeutic measure such as intravenous therapy and suction decompression. In 1940, the mortality rate in most large clinics was 20%. Wangenstien was the first to publish figures in this range.

A comparison of recent reports highlights the controversy about early operation. Moses operated on 75% of patients with an operative mortality of 8%. Eliason operated on 90% of patients with an operative mortality of 11%. These figures represent definite reductions from former years. There are two lessons to be learned from this; first, it would seem that within certain recognized limits, the important thing is not *what* is done but *how* it is done. The skill of the surgeon plays a major role in determining the outcome; second, we see that there was nothing gained by a higher operation rate, implying that many patients would get well with conservative treatment as well as with operative treatment. It is understandable that many men hesitate to rely on intubation alone because in the past it has been used to hide ignorance and indecision rather than to fulfil a specific purpose. However, it is hoped and believed that use of sulphonamides and penicillin will eliminate much of the danger attendant on longer observation and conservative management, as well as aiding in surgical treatment.

The author wishes to express his thanks to Dr. Jessie Grey for her help in the preparation of this paper.

THE HEART IN PREGNANCY

By J. M. FINLAY, 4T7

INCLUDING:

I: *A sketch of the changing relationship of cardiology to obstetrics in the last 70 years.*

II: *The physiological circulatory changes occurring in the normal woman, during pregnancy.*

III: *The circulatory changes occurring in the woman with heart disease, during pregnancy.*

I: HISTORY:

The need for a discussion of the circulatory changes occurring during pregnancy, in the normal woman and in the cardiac patient, becomes obvious, when one considers that:

The first careful attempt to correlate heart disease and pregnancy was published only 68 years ago, in 1878, and as late as 1921, the understanding of heart disease in pregnancy, as presented in the current obstetrical text-books and teachings, was outdated by at least 50 years.

In 1878, a London physician, Angus MacDonald, published the carefully collected data of his findings in 31 of his own patients who suffered with heart disease in pregnancy. Unfortunately, his observations went more or less unheeded, and textbooks before 1900 contained only scanty, vague and gloomy remarks about the heart. Some texts, however, did quote MacDonald and his 55% death rate, and also Peter, who in a publication in 1874 advised cardiacs not to marry, not to bear children, and if they did, not to nurse them!

At the turn of this century in 1899, Hirst, in his textbook gave a death rate of 50% in pregnant cardiacs, and advised that all cardiac patients be interrupted not later than the 36th week of gestation.

From 1900-1920, although the obstetrical textbooks still gave scanty space to heart disease, and made vague suggestions supported by meagre statistics, the attitude towards prognosis became less gloomy. In the 1912 edition of Williams' Obstetrical textbook, heart disease was doubted to be as dangerous as was the common belief, and was guessed to occur once in several hundred cases. But the remarks were confined to only two pages and clearly did not grasp the problem, —nor did any of the texts used before 1931.

Sir James Mackenzie, who published "Heart Disease and Pregnancy" in 1921, complained that modern medical knowledge of heart disease was poorly understood and taught. He also stated that in textbooks on obstetrics and in discussions on heart disease in pregnant women, the "views expressed were not as recent as when Angus MacDonald published his treatise in 1878."

Although this state of affairs regarding textbooks existed until 1931—the obstetricians themselves, who were beset by women appearing in the latter part of

pregnancy in severe cardiac decompensation, necessarily began centering their attention on methods for delivery of such patients. It seemed,—and perhaps rightly so, under the current conditions,—that prompt delivery was the only hope for survival in these patients, and that Caesarian Section was the safest method.

In 1920, Doctor Newell of Harvard Medical School, started special services for the study of some of the complications of pregnancy, including heart disease. A heart clinic was organized at the Boston Lying-In Hospital by the end of 1921 and clinical studies were begun by Doctor B. E. Hamilton. The patients who arrived there created the problem of "heart disease in pregnancy," and the realization of the need for the following facts:

The precise rules we now have for the selection and treatment of pregnant cardiac patients.

The methods of their delivery.

The accumulation of the vital statistics, on which the prudent cardiac patient can now decide whether or not she will risk a pregnancy.

The rules for the selection and treatment of pregnant cardiacs are nearly all the direct result of Out Patient and bedside care and study by practitioners of large numbers of women of child-bearing age who are cardiacs. The present low maternal mortality of cardiacs can be credited mainly to these rules. Coupled with this, the physiological studies of the circulation in normal pregnant women, simplified for bedside use, has led to new discoveries regarding the time during pregnancy when heart failure makes its first appearance, and, has had direct bearing on methods for delivery.

One of the outcomes of the above is that it is now no longer considered to be a sound rule to interrupt pregnancy several weeks before term, because of the fear of a mounting load on the heart, in severe cardiacs. Fewer interruptions mean fewer Caesarian Sections. Their number has been further reduced by the obstetrician's growing dislike of operative delivery through the abdomen, when there are no obstetrical contraindications for delivery through the pelvis. It is of interest to note that it was not until 1933 that the Obstetrical Department of the Toronto General Hospital stopped doing Caesarian Sections for heart failure.

During the period 1922 to 1941, many physiological studies were made by Dr. B. E. Hamilton at the Boston Lying-In Hospital, and it is from his book, that I have gleaned most of the following material.

II: The Physiological Circulatory Changes Occurring in the Normal Woman During Pregnancy:

Accumulated evidence indicates that pregnancy imposes a "burden" on the maternal circulation. It has been noted in patients who had been diagnosed "favourable" cases for the trial of pregnancy, in whom heart failure had never before occurred, that 20% decompensated during pregnancy. Also, if such patients survive pregnancy, and do not become pregnant again, they live for many years without recurrence of congestive heart failure. Thus, knowing that alterations in the physiology of circulation are great enough to produce such significant effects on

the circulation of patients with diseased hearts, it is to be expected that pregnancy in normal women, would produce recognizable changes in the hemodynamics of circulation. That these changes do occur in the normal, has been confirmed by laboratory observations and physiological studies.

In pregnancy, therefore, the differentiation between women with normal, and with diseased hearts, is complicated by the normal symptomatology produced by these changes. Normal pregnant women frequently complain of dyspnoea on exertion, and many are orthopnoeic, especially in the latter half of pregnancy. A large number are awakened at night, by attacks characterized by choking, palpitation and respiratory distress—often suggesting attacks of nocturnal dyspnoea. Palpitation, tachycardia and irregular heart action (extrasystoles) are not uncommon complaints. Swelling of the legs and even of the hands, is common. These symptoms may occur singly or in combinations, and may be of sufficient severity to suggest cardiac insufficiency.

Should the heart of a patient with some of the above symptoms be borderline in size, and show, on physical examination, a loud apical systolic murmur, and an apex beat somewhat more vigorous than usual, it is understandable why one, unfamiliar with the normal pregnant woman, might be led to make an erroneous diagnosis of heart disease.

In addition to the above findings, the skin may be flushed, the pulse somewhat collapsing in type; capillary pulsations may be found in the nail beds, and the superficial veins over the chest and abdomen may be prominent and distended. The neck veins often become prominent and the pulsations may be increased. Frequently, there is demonstrable oedema of the lower extremities, and slight generalized puffiness of the subcutaneous tissues. Occasionally, transient râles occur at the lung bases, which may be cleared by deep breathing or coughing—i.e. they are "atelectatic." As pregnancy progresses, the heart is often displaced upwards and to the left, so that the apex beat may be in the fourth left intercostal space, and the left border of dullness at, or outside, the mid-clavicular line.

The purpose of the following studies of the circulation is to attempt to elicit the source of these normal symptoms; to relate them and their quantitative changes to the progress of pregnancy, and to indicate which of these findings may be important in the diagnosis of heart disease in pregnancy.

(a) *Changes in the Size, Shape and Position of the Heart in Pregnancy:*

The area of cardiac dullness, and the size of the cardiac shadow by X-ray and fluoroscopy, in some cases, can increase in pregnancy. However, if either hypertrophy or dilatation of the heart, or both—(that is, a change in size)—occur in the course of normal pregnancy, the evidence thus far has been inconclusive. Numerous conflicting reports are to be found in the literature. Certainly, experimental studies on animals, do not support this contention.

In the light of the above, it seems more rational to consider changes in the shape and position of the heart in relation to the chest diameters, than changes in cardiac size. Changes in the relationship of heart, chest and diaphragm do occur,

which are sufficient to account for changes in the cardiac shadow. These observations are further substantiated by electrocardiographic evidence of change of position and shape in the form of left axis deviation and inverted T_3 waves in normal pregnancy.

That pregnancy, per se, increases the work of the heart cannot be doubted, however, no significant enlargement of the sound heart can be accounted for, in any number of normal uncomplicated pregnancies. Nevertheless, it is possible in women with heart disease, that the burden of pregnancy sometimes results in significant increase in heart size, but this practically never occurs in the absence of congestive heart failure.

(b) *X-ray Studies of the Thorax in Pregnancy:*

In nearly all cases, X-rays of the chest during the latter two-thirds of pregnancy reveal an increase in the normal lung markings which may be mistaken for abnormal pulmonary congestion. Post-partum this change disappears. Histological studies by Hofbauer, revealed that the changes were due to an increase in the size of the pulmonary vascular bed. Although this pulmonary congestion might be expected to decrease vital capacity, there is a compensatory increase in vital capacity brought about by changes in the chest configuration and diaphragmatic relationships:

I: The transverse diameter of the chest increases antepartum and decreases post partum.

II: The circumference of the chest and subcostal angle increase antepartum and decrease post partum.

III: The diaphragm is pushed up to a higher level antepartum but its function is not appreciably altered.

Since vital capacity does not normally decrease in pregnancy, a significant decrease (10% or more) must be explained by some pathological state.

(c) *Dyspnoea in Pregnancy:*

Dyspnoea cannot be explained by a decrease in vital capacity. Satisfactory explanation of its production lies in the fact that dyspnoea depends largely on the ratio between vital capacity and pulmonary ventilation. A large increase in pulmonary ventilation with only a relatively slight increase in vital capacity would, therefore, lead to dyspnoea. This is precisely what occurs in pregnancy. Anthony and Hanson have shown that there is a 57% increase in pulmonary ventilation, and Hasselbach has shown that the irritability of the respiratory centre is heightened, during pregnancy.

On standardized exercise, the respiratory rate accelerates more readily in pregnancy, than in the non-pregnant state.

(d) *The Arterial System in Pregnancy:*

No recognizable structural alterations in the general arterial system have been found in pregnancy. However, the arterial supply to the uterus is known to be

altered. Spanner demonstrated that the placental arteries connected with the veins through large vascular spaces, without the interposition of arterioles or capillaries. These arterial changes in the maternal part of the placenta show certain similarities to a modified arterio-venous fistula. For example:—after the repair of an arterio-venous fistula, the pulse rate decreases. It has been observed in some cases, that the pulse rate which increased antepartum, abruptly decreased coincident with the delivery of the placenta, during Caesarian Section.

For the remaining circulatory changes, it will probably be an aid to visualization, to refer to the following chart. (figure I.) This chart shows the average curves of quantitative change in relation to the particular time of progress of pregnancy. Each curve represents the changes observed in the various physiological phenomena to be described,—in both the antepartum and post partum periods, Note that the time antepartum is measured in months, and the post partum, is measured in weeks.

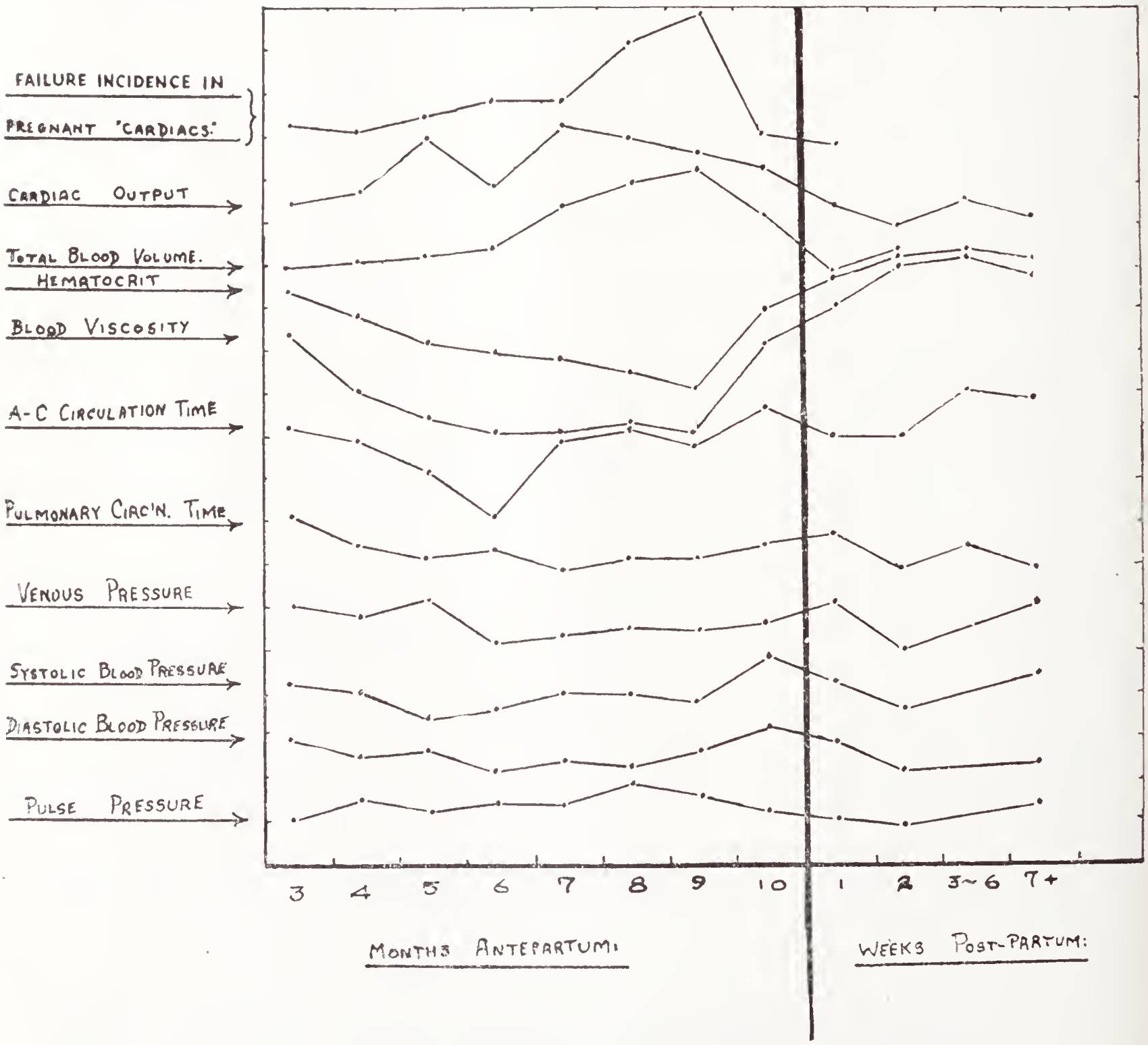

Fig. 1. (After Hamilton and Thompson)

(e) *The Arterial Blood Pressure in Pregnancy:*

The basal arterial blood pressure remains within normal limits (S/D 140/90) during pregnancy in the normal woman, but it presents considerable variation from month to month. There is a tendency for both the average systolic and diastolic pressures to decrease, from the fourth through the ninth lunar months, and to increase during the tenth lunar month. There is, however, a disproportionate decrease between the two which results in an increase in the pulse pressure.

The antepartum changes in blood pressure are associated with the clinical signs of flushing of the face and extremities, a collapsing pulse, and often capillary pulsation in the nail beds.

These blood pressure changes are thought to be due in part to:

I Peripheral vasodilatation.

II The arterio-venous leak in the placenta.

(f) *The Superficial Veins in Pregnancy:*

The superficial veins over the breasts and abdomen are more readily seen by infra-red films, because of engorgement and the stretching of the skin over them, in pregnancy. No new channels are formed, in contra-distinction to what occurs in portal cirrhosis.

(g) *The Venous Pressure in Pregnancy:*

I *In the Arm:* The arm venous pressure remains within the normal range of two to twelve centimetres of water during pregnancy and the puerperium in normal women. Slight variations from month to month indicate that pressure tends to increase early in pregnancy, decrease towards term, and increase slightly again in the puerperium.

II *In the Leg:* Although the arm and femoral venous pressures are approximately equal in non-pregnant individuals, in pregnancy, the femoral venous pressure is elevated. It is high late in pregnancy, as compared with early pregnancy and the puerperium.

Burwell has indicated that this increased pressure is probably due to two factors: first; the mechanical pressure of the enlarged uterus on the iliac veins with partial obstruction to flow, and second; the discharge of blood into the iliac veins under higher pressure than normal, as a result of the placental circulation, (i.e. resembling an arterio-venous fistula).

This increased pressure in the lower limbs is no doubt a factor in the production of oedema and varicosities during pregnancy.

(h) *The Effect of Rapid Intravenous Fluid Administration in Pregnancy:*

Observations on the effect of rapid intravenous infusion of normal saline have been made on normal pregnant women paying special attention to arm venous pressure, arterial blood pressure, pulse rate, respiratory rate, blood hematocrit, and hemoglobin and erythrocyte count changes.

After the intravenous injection of 1500 cc. of normal saline in from 30 to 40 minutes, it has been found that:

I Arm venous pressure gradually increased, and then decreased to basal level in 10 to 20 minutes.
II Arterial blood pressure remained essentially constant.
III Pulse rate is uniformly accelerated by about 15 beats per minute over the basal level.
IV Respiratory rate usually increases several cycles per minute, and sometimes subjective dyspnoea occurs.
V Venous blood hematocrit decreases 10 to 20%.
VI Erythrocyte count and hemoglobin estimation decrease correspondingly.
VII Vital capacity decreases.

The changes in each of the above were not uniform during the antepartum and post partum periods, but showed a greater degree of change up to the ninth lunar month, and following this, a lesser degree.

The untoward effects that may be produced by rapid fluid administration to normal pregnant women with sound hearts are of obvious importance. They serve to emphasize the great care that must be exercised in fluid administration to pregnant cardiacs, particularly during that period of pregnancy when the burden is maximal.

(i) *The Oedema of Pregnancy:*

Clinically recognizable oedema occurs in about 27% of normal pregnant women, as shown by studies by Hamilton, and by Landt and Benjamin. It may occur early in pregnancy (6 months or before), but is most often present during the last two months. It may be generalized, but is usually localized to the lower extremities and vulva.

The factors concerned in oedema production are probably multiple:

I Increased venous pressure in the iliac veins leading to increased capillary pressure in the lower extremities and vulva.
II Slight diminution in plasma proteins resulting in decreased osmotic pressure.
III Marked increase in blood volume (i.e. "hydration") which dilutes the osmotically-active blood substances.
IV Possibly, disturbances of lymph drainage, particularly from the lower extremities.

There is no evidence of a renal factor, or of increased capillary permeability, in normal pregnancy.

(j) *The Velocity of Blood Flow in Pregnancy:*

The arm-to-carotid (A/C) circulation time, utilizing the pathway between an antecubital vein and the carotid sinus, has been found to increase at about the 17th week of gestation, to remain increased till the 36th week, and then to decrease again, just prior to term. It then increases post partum, and finally returns to normal by the 7th post partum week.

The pulmonary circulation time has been found to show no appreciable change. This is thought to be due to the great increase in size of the pulmonary vascular

bed during pregnancy, which permits a larger volume of blood to flow through it in unit time, without an increase in the velocity of flow.

The venous circulation time is simply the arithmetical difference between the A-C circulation time and the pulmonary circulation time. Since the latter is constant, the venous circulation time varies almost directly with the A-C circulation time.

The speeding of the circulation in pregnancy, therefore, appears to occur primarily in the peripheral part of the circulatory pathway and not in the pulmonary circuit. This increased velocity is thought to be accompanied by an increase in cardiac output, and a decrease in blood viscosity.

(k) *The Blood Volume in Pregnancy:*

There is a progressive increase in the total blood volume, from early in pregnancy to the ninth lunar month, at which time, the average increase was 45.5% over the average of a comparable normal, non-pregnant, control group. During the tenth month, there is a definite decrease in total blood volume, with a prompt return to normal limits by the second week of the puerperium.

The factors which produce these changes observed in the blood volume during pregnancy are not clear. The simplest explanation is that more maternal blood is required during pregnancy to fill the vascular bed, enlarged by the addition of the placenta. But this in itself does not explain the magnitude of the increase. The disturbances in water balance, and other changes in pregnancy, resembles those seen in various types of endocrine dysfunction,—especially the blood volume changes. This suggests that the underlying mechanism controlling blood volume during pregnancy is on a hormonal basis. Support for this view has been demonstrated by Thorn and Harrop, in that both androgenic and oestrogenic substances exert a retentive effect on water and sodium.

(l) *The Peripheral Blood in Pregnancy:*

Hematocrit readings, erythrocyte counts and hemoglobin estimations made on peripheral blood, show an inverse relationship to the plasma volume, during pregnancy.

Cohen and Thomson found that the blood viscosity decreases as pregnancy progresses, and reaches a minimum viscosity at the ninth lunar month, when the total blood volume is maximal. It then commences to return toward normal, becoming more viscid in the tenth lunar month, and continuing in this direction in the puerperium.

(m) *The Sedimentation Rate in Pregnancy:*

The sedimentation rate of the red blood cells is much increased over normal during normal pregnancy. The increase begins as early as the tenth week and continues throughout gestation. It is probably closely connected with disturbances in the blood protein level,—particularly in the fibrinogen and globulin levels.

(n) *The Cardiac Output, in Pregnancy:*

Both the total cardiac output and the output per beat (i.e. the minute and stroke volumes respectively) are increased in pregnancy. The former by an average of 40 to 50%, and the latter, by an average of 10 to 20%. Thus, the increased work imposed on the heart during pregnancy is not performed merely by increasing the heart rate,—the actual work per beat must also increase.

The heart of the normal pregnant woman, while at complete rest, obviously then, does more work than that of a normal non-pregnant woman, under similar conditions. As well, Schmidt has observed that during exertion, there is a disproportionate increase in the cardiac output, as compared with the increase that similar effort produces in the normal non-pregnant woman.

Hence, the pregnant woman, is in a state of double jeopardy as far as her circulatory burden is concerned—(more work, and an excessive increase with effort). It is little wonder, then, that the pregnant woman whose cardiac reserve is already diminished by heart disease, is so likely to develop cardiac decompensation under the physical and emotional strain of pregnancy.

With knowledge of the above facts, it is obvious that one cannot predict early in pregnancy, whether a given patient is a good obstetrical risk or not. It is far more important to know what *physiological load* a given heart may be expected to carry as pregnancy progresses, to *anticipate* this load, and to *compensate for it* by careful regulation and restriction of the patient's daily activity.

To do this, it is necessary to consider the nature of the circulatory burden, and its relationship to the *duration of gestation*. From the individually discussed aspects of the circulation in pregnancy, one important fact stands out,—that the phases of the circulation studied show definite trends which correlate remarkably with each other, both in direction, and in relation to the duration of pregnancy.

Thus, the factors which contribute most to the circulatory burden during pregnancy; i.e. 1 Cardiac Output
2 Blood Volume
3 Blood Velocity
4 Blood Viscosity
5 Hematocrit

—change in such a way that the resultant burden increases slowly, early in pregnancy; rapidly from the fifth month until the maximum is reached in the ninth lunar month; and most significantly, each returns toward normal during the final weeks (the tenth lunar month) of pregnancy. The circulatory load, then, does not, as had been previously believed, progressively increase, to reach a maximum at term. Rather, the maximum is reached, on the average, between the 34th and 36th week. Why the tenth month changes are effected, is not completely clear. It may be associated with:—I. Cessation of the growth processes in the foetus; or II. Changes in the mechanical relationships of the uterus to the diaphragm and pelvis, which may occur at this time (i.e. "Lightening")

There now remains to indicate how these laboratory observations correlate with clinical facts:

A. With the above concept of the circulatory burden, it would be expected that in patients with diminished cardiac reserve, few would develop cardiac decompensation early in pregnancy; the numbers would increase during the period when the circulatory burden is increasing in magnitude; would be most during the period when the load of pregnancy is at its peak; fewer in the final weeks of pregnancy as the burden diminishes; relatively few during delivery; and almost none in the querperium.

This is exactly what has been found to happen among cardiac patients.

B. Likewise, improvement in circulatory function might be expected in the final weeks of pregnancy, in patients who are in chronic heart failure, while at bed rest, and under optimal medical treatment.

This again is exactly what happens.

Therefore, it can now be stated that knowing not only that these changes *do* occur, but also, *when* they occur, is essential in the management of the pregnant woman with cardiac disease.

To Summarize:

1. Proper evaluation of the cardiovascular status of the normal pregnant woman with especial reference to signs and symptoms, is necessary, in order to avoid erroneous diagnoses of heart disease in normal pregnant women, and, of heart failure, in pregnant women with cardiac disease. Incorrect interpretation of changes in the electrocardiogram, or X-rays of the chest during pregnancy, may also lead to errors in diagnosis.

2. A consideration of the hemodynamic changes accompanying normal pregnancy yields adequate physiological explanation for the occurrence of heart murmurs, oedema, dilatation of superficial veins, capillary pulsations, and other seemingly abnormal signs.

3. The major alterations in the circulation of normal pregnant women include the following: a)—An increase in the circulating blood volume; b)—An increased cardiac output; c)—An increased velocity of blood flow; d)—An increased pulse pressure; e)—An increased heart rate and f)—A decrease in hematocrit, viscosity, hemoglobin and erythrocyte count per unit volume of circulating blood. The correlation of these factors with the temporal relation of their change to the duration of gestation has been indicated.

4. Whatever the mechanism, the circulatory changes described allow for a greatly increased maternal blood flow through the placenta. These changes raise the question as to whether or not the placenta is a modified arterio-venous fistula. (The following characteristics common to both pregnant women and patients with large arterio-venous communications strongly indicate this possibility; a)—Tachycardia; b)—Increased pulse pressure; c)—Increased blood volume; d)—increased cardiac output; e)—elevation of venous pressure in the veins adjacent to the fistula, and f)—a continuous bruit over the area of the anastamosis, with systolic acentuation.) However, at present, it is impossible to acount for all changes in preg-

nancy on this mechanical basis, especially, for the time of change,—so that hormonal and other factors are thought to play some role.

5. The physiological adjustment of circulation during pregnancy—particularly, the increase in blood volume, cardiac output and velocity of blood flow,—appear to be the significant factors which predispose the pregnant cardiac to heart failure.

6. Physiological, as well as clinical observations, indicate that heart failure in early pregnancy may be expected to grow worse, as the circulatory burden increases, and to improve during the final weeks of pregnancy as the circulatory burden diminishes.

III. The Circulatory Changes Occurring in the Woman With Heart Disease During Pregnancy:

It has been indicated that some of the alterations associated with severe congestive heart failure in the non-pregnant individual, may be physiologically present in normal pregnancy.

In order to appreciate the significance of circulatory changes in heart failure during pregnancy, it is necessary to have a basic knowledge of how the compensated cardiac patient behaves under the duress of gestation. A cardiac patient in pregnancy has been defined by Hamilton, as "a woman whose heart may cause death or disability during pregnancy or the puerperium."

For this study, cardiac patients may be divided into two groups:

A: Those with major cardiac disease who remain compensated during pregnancy.

B: Those with major cardiac disease who developed cardiac decompensation. Using the same methods of study on the same phenomena as in the previous section, observations were made on these two classes of cardiac patients. Significant changes occurred in only *two* respects, *Vital Capacity,* and *Blood Volume,*—and both of these occurred only in those patients who developed *decompensation.*

1. Vital Capicity:

Carefully determined vital capacity readings done at frequent intervals on the same patient during pregnancy are of distinct value in the diagnosis of impending congestive failure, before it becomes manifest by usual clinical means.

Vital capacity shows a sudden decrease before congestive failure occurs. A decrease of 15% or more, or a continued decrease from month to month of 10% or more, is thought to be a definite sign of impending heart failure in a pregnant cardiac, in the absence of some other obvious extracardiac cause. The amount of the decrease, and not the absolute value of the vital capacity, is the significant factor in the use of vital capacity as an aid in the diagnosis of subclinical heart failure. (figure 2).

2. Blood Volume:

Even in pregnancy, when there is normally a tremendous increase in blood volume, congestive heart failure is accompanied by a further increase over the average values for normal pregnant women for that particular period in question.

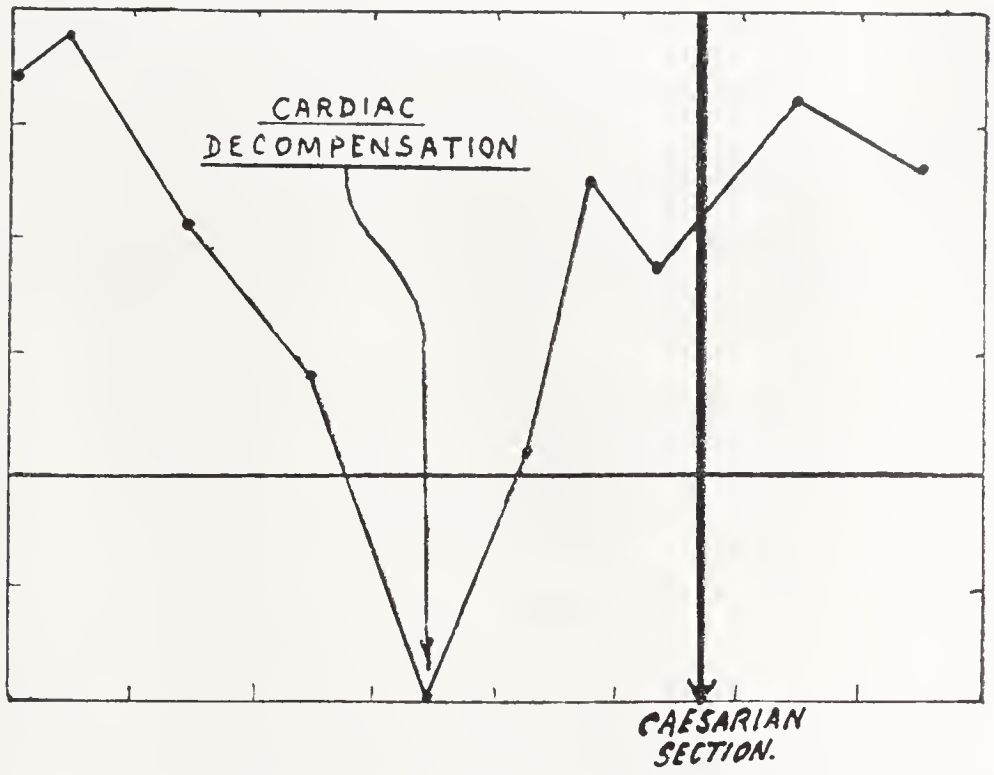

Fig. 2. Vital Capacity Changes. (After Hamilton and Thompson)

And, improvement in, or disappearance of heart failure is characterized by a decrease in blood volume towards the normal level for that particular period of pregnancy. (figure 3)

(Note the increase over the expected "normal" (dotted line) during cardiac decompensation. With restoration and maintenance of compensation during the remainder of pregnancy, the course of the blood volume parallels the average curve for normal pregnant women.)

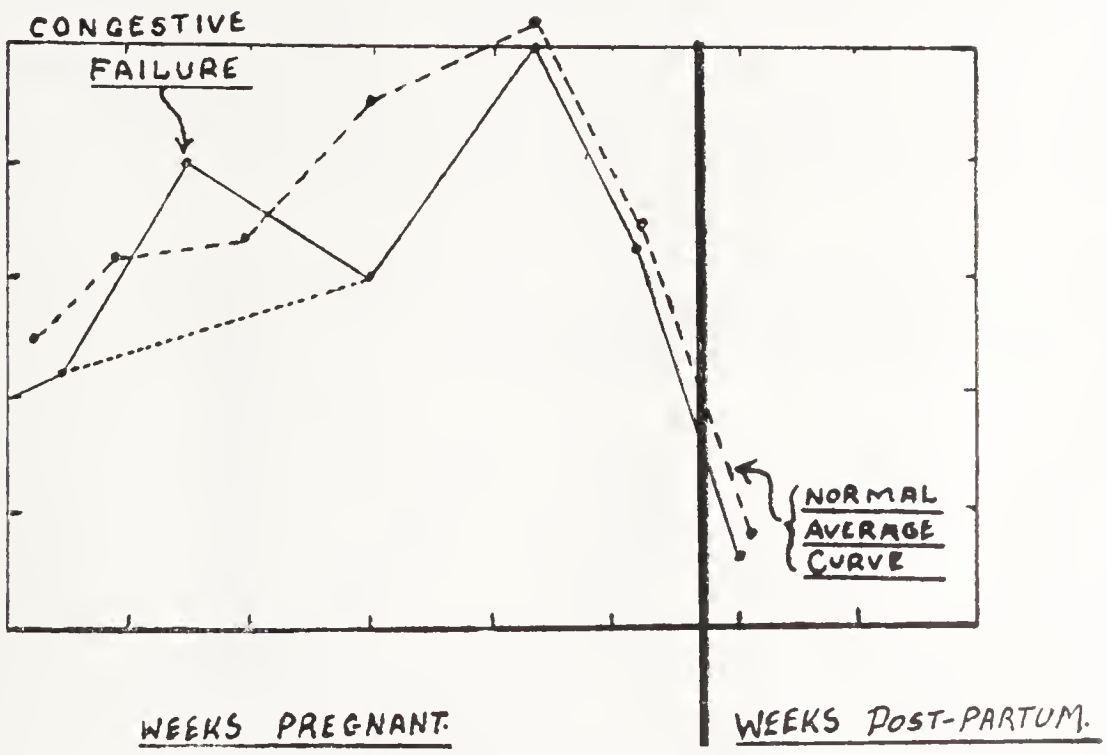

Fig. 3. Blood Volume Changes. (After Hamilton and Thompson)

Summary

1. The compensated cardiac does not behave significantly different from the normal pregnant woman, as far as changes in circulatory hemodynamics are concerned.

2. Patients with congestive heart failure did not show striking deviations from the normal in most phases of hemodynamics studies, but it was found that early convestive heart failure is accompanied by: a)—a significant increase in total blood volume; b)—a significant decrease in vital capacity.

3. Vital capacity observations prove to be of definite clinical value in detecting early congestive heart failure, antedating other evidence of pulmonary congestion by several weeks.

4. The combination of decreased vital capacity and increased blood volume favors the production of pulmonary oedema. This is fortunately so, because it provides a clinical means of the next earliest and most accurate detection of heart failure in the pregnant cardiac.

5. Recognition of the young cardiac is still based on direct examination and history taking.

In respect to the broad general outlines of treatment, consideration of the curve of failure incidence, which may also represent the curve of the cardiac load, leads to the following conclusions:

a) The load may change rapidly. Good condition at one visit does not insure good condition later, even if the same regimen is maintained. A cardiac must be watched closely throughout pregnancy, but particularly, when the load grows heavier.

b) Special care for the pregnant cardiac is even more necessary in the period from the sixth to eighth month, than in the last month, although essential at all times.

c) If a cardiac fails during the sixth, seventh or eighth months, should pregnancy be interrupted? It will not immediately improve the failure. It imposes additional strain, when there is a heavy burden already. This burden will lighten normally toward term. It seems a better policy then, to make every effort to keep the patient alive, and to wait for his automatic lightening.

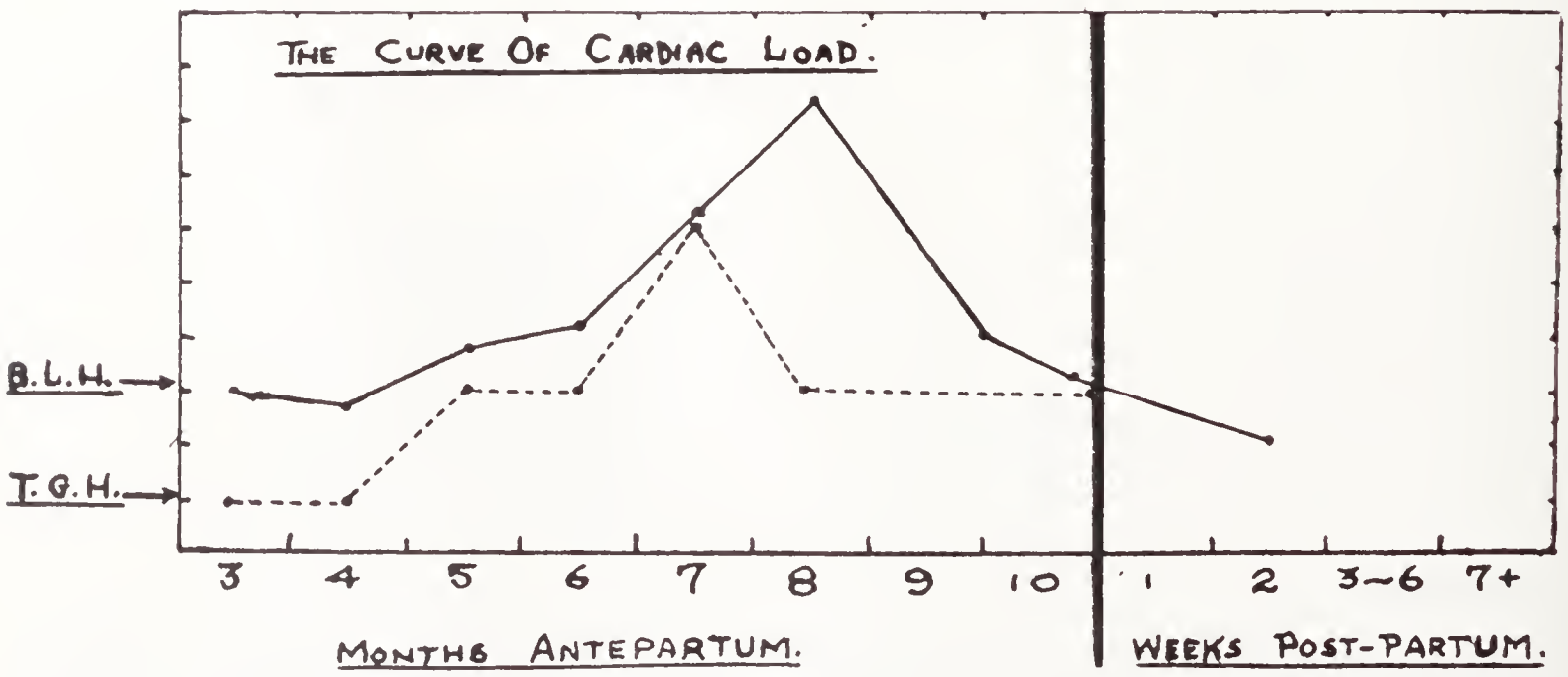

Fig. 4.

A Comparative Study Of Failure Incidence At The Toronto General And Boston Lying-In Hospitals: (figure 4).

At the Toronto General Hospital, of 33 patients studied, who decompensated during pregnancy, 22 showed records of the time of onset. It is from these that the second curve is taken (Fig. 4.). The similarity between the two is obvious, except that in the Toronto General Hospital records, maximum incidence occurred between the sixth and eighth lunar months.

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METHANOL POISONING

J. W. DALES, 4T8

Definition

Methanol is the official name for methyl alcohol, CH_3OH, wood alcohol and methyl hydrate.

Pharmacology

Methanol can be absorbed in toxic amounts through the skin, the lungs and any mucous membrane.

The average fatal dose is 60 mils but varies from 30 to 200 mils. This variation is due to individual differences in metabolism. Methanol is not fully oxidised in the body but is broken down into formaldehyde and formic acid. The oxidation is very slow and formic acid may be found in the urine for 6-8 days. Opinion varies as to whether the poisoning effect is due to the alcohol, the formaldehyde, or the formic acid. In any case, treatment directed against the acidosis has proved the most effective.

It seems that the intoxicating power of alcohols increases with the number of carbon atoms while the poisoning effect varies in the opposite direction. The person who drinks Methanol with intoxication as his aim is very disappointed. Unfortunately, the same cannot be said of its lethal effect.

Pathology

Death is the result of respiratory paralysis.

On inspection, the victim presents a pinkish red postmortem lividity involving the face, neck, shoulders, abdomen and thighs.

The brain is slightly edematous and the content of methyl alcohol is sufficient to cause death. The blood is unclotted and a dark brown colour. There is engorgement of all viscera and fatty infiltration of the liver and kidneys.

Sources of Methanol

As a beverage—In these cases the patient is usually under the impression that anything labelled alcohol is for consumption. Addiction has been reported but it must be very rare. The chronic alcoholic may obtain methyl alcohol from drinking patent preparations. In some countries, it is illegal to use methyl alcohol in any proprietory preparations. In Ontario, it may be used in certain amounts if the mixture is properly labelled.

As an industrial hazard—In industry methyl alcohol is used as a cleaning agent and paint solvent. Poisoning is not a rare occurrence. The alcohol may exist as a vapour or a liquid and is absorbed through the lungs or the skin. It is reported that the use of a shampoo containing methanol has caused toxic symptoms.

Chronic Methanol Poisoning

The slow elimination and its accumulative effect favour chronic poisoning.

Local effects—Methanol irritates the conjunctiva and causes dryness and hyperemia of the skin.

General effects—The eye disturbances consist of dilatation of the pupils, loss of accommodation and finally blindness. In the lungs, it is frequently a cause of bronchopneumonia. Digestive upsets and cystitis may occur. In the nervous system, it produces headache, tinnitus, trembling, neuralgia, neuritis, staggering, coma and death.

Acute Methanol Poisoning

The symptoms vary in different patients. Some of the symptoms are blindness, severe chills, dyspnea, cyanosis, weakness, intense abdominal pains, irrational conditions, headache, paresthesia, staggering, convulsions and coma.

Because of the variability of symptoms, Kobra finds that the course of the illness is more important and more constant. He describes four phases.

1. Period of drinking. The immediate inebriation is slight.
2. Latent period. This lasts for 12-24 hours. The patient may feel fine or may have some general discomfort such as headache, nausea, or vomiting.
3. Acute stage. The first sign is a blurring of vision which may rapidly pass to blindness. At this stage edema and congestion of the optic discs may be seen. A reduction of consciousness occurs which may pass quickly to deep coma. The breathing is of the Kussmaul type.
4. Circulatory insufficiency. Cyanosis and coldness of the periphery are terminal symptoms. The patient may die in a few hours once he has entered the third phase.

Diagnosis

When a history is obtained, diagnosis is no problem.

If the patient is found in coma, diabetic coma must be considered. The following points help the differentiation.

1. The changes in the fundi are specific for methanol poisoning and are not found in diabetes.
2. Methanol poisoning does not cause a glycosuria.
3. The course is much more rapid in methanol poisoning.

Laboratory findings indicate a severe acidosis. The carbon dioxide combining power of the plasma is reduced and varies from 6 to 20 vol. %. The pH of the blood is normal or slightly reduced. There are large amounts of formic acid in the urine. This acidosis is considered to be the focal point in methanol poisoning and the cause of death. (1)

Treatment of Acute Methanol Poisoning

Effective treatment has been singularly lacking until one year ago. Previous treatment has consisted of circulatory and respiratory stimulants, intravenous saline, gastric lavage and purgatives. Treatment directed at the severe acidosis has been very successful. (1, 2)

Both sodium lactate solution and sodium bicarbonate have been used with equally good results. For intravenous injection, the lactate solution is preferable

as it yields the sodium more slowly into the system and thereby lessens the possibility of an uncompensated alkalosis. Release of sodium occurs as the lactate is metabolised.

If the patient is conscious he may be given 30 gm. of sodium bicarbonate by mouth.

If the patient is unconscious, the same amount of sodium bicarbonate may be given through a stomach tube. This should be supplemented by intravenous therapy. If sodium bicarbonate is used, Kobra recommends 6-12 gm. of a 5% solution. If sodium lactate is used, Chew et al recommend 120 cc. of sodium r-lactate solution molar in 1 litre of isotonic solution of three chlorides. In our hospitals, the solution of lactate which is available is 1/6 molar solution of sodium r-lactate. Seventy cc. of this solution corresponds to 1 Gm. of sodium bicarbonate. Initial treatment should consist of 1,000 cc. of this solution with more as required.

As elimination of Methanol is slow, small doses of sodium bicarbonate are continued until the patient is well. The response is followed by the carbon dioxide combining power of the plasma or the reaction of the urine. Alkali is given until the carbon dioxide combining power is normal or the urine has become alkaline.

Response to this therapy is dramatic. Within a few hours dyspnea, nausea and mental symptoms abate. Most patients show an improvement or disappearance of eye symptoms but in severe cases there may be no improvement.

Summary

Methanol is a very toxic substance small amounts of which are fatal. After ingestion of a lethal dose, the patient passes through a latent period of 12-24 hours during which he may suffer only mild discomfort. Following this, he quickly passes into coma and dies from respiratory paralysis. The clinical picture indicates acidosis. Treatment of this acidosis has been the only successful therapy.

The author wishes to express his thanks to Prof. Ferguson of the Dept. of Pharmacology and to Mr. O'Sulivan of St. Michael's Hospital, for their help in the preparation of this article.

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TECHNIQUES OF TUMOUR TRANSPLANTATION

IAN ALGER 4T9

Introduction

At the present time more people are dying of cancer than ever before. While it is true that this increase may be more apparent than real because of a general increase in the age of the population, research workers everywhere are investigating with renewed interest the nature and causes of malignant tumors. There are at least two reasons for this heightened interest. The first is that considerable amounts of money have been made available for research purposes. The second reason is to be found in the many recent advances in the basic sciences which for the first time have made possible a satisfactory study of the cancer problem.

We all realize that environmental conditions play a large part in determining our behaviour. In different situations, different aspects of our character become apparent. A mild and peaceful storekeeper becomes a dangerous fighter when a robber tries to steal money from his cash register. The bravery of a previously insignificant elevator operator is recognized when he remains at his post when the building takes fire. Now cancer cells in the body might be compared to people. While the cells are growing in the body they may not exhibit all their characteristics, just as people in a given situation do not show all aspects of their nature. If the cells could be made to grow under other environmental conditions, however, a new understanding of their essential constitution might be gained. With this last premise in mind, tumor cells have been transferred from one animal to another; they have been grown in tissue cultures and in the anterior chambers of the eyes of animals, and in the yolk sac of the developing chick embryo. A brief discussion of the various techniques of transplantation will be presented in this paper.

Transfer From one Animal to Another

The difficulties one encounters in transplanting tissue from one animal to another are great. These same difficulties are present when tumor tissue is used instead of normal tissue. In order to overcome this problem, strains of animals were inbred for over one hundred generations and these brother and sister matings resulted in animals which, for the purposes of transplantation, were identical. Thus, tumors can be carried in these animals and can be transferred from one to the other with great ease.

Tissue Culture

The whole technique of tissue culture cannot be said to be more than 35 years old, and as yet only a comparatively small number of investigators have studied the behaviour of isolated tumor cells. The culture medium used in the cultivation of the cells has two components. One is the supporting element, which in the case of the plasm culture is fibrin, and the other is the growth promoting element. Various problems have been investigated by this technique, and they include the

question as to whether or not the cells retain their malignancy *in vitro* and whether malignant cells can be produced *in vitro* by the use of carcinogenic agents. The real significance of this method of investigation has been summed up by Parker who has written, ". . . as cancer workers come gradually closer to the real cause of malignancy, it is almost certain that tissue culture will serve as one of their most valuable tools."

Anterior Chamber Transplants

The original work along this line was done by Greene of Princeton in 1938. Previously it had only been possible to transplant a tumor to another member of the same species, but the ease with which homologous transfer of rabbit tumors to a transplantation site in the anterior chamber of the eye was accomplished when

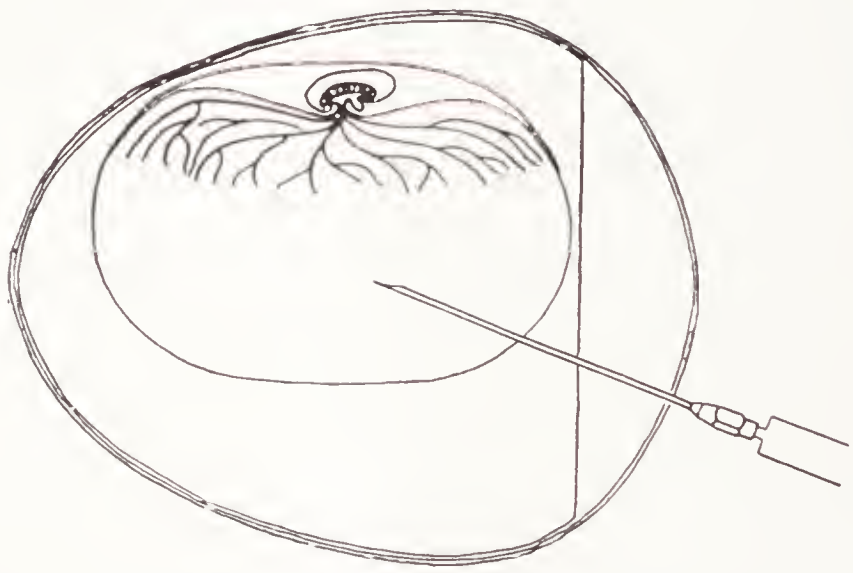

Fig. 1. *Method of injection of tumor tissue into the yolk sac of a developing chick embryo.* The upturned needle is seen passing through a hole in the outer shell, traversing the air space, piercing the inner shell membrane, and entering the yolk sac itself.

implantation in all other regions failed, led Greene to believe that this might be a technique which would allow transfer of tumors between animals of different species.

The technique used by Greene was very simple. A tumor, such as a spontaneous adenocarcinoma from the endometrium of a rabbit's uterus, was transplanted to the anterior chamber of the eye of a guinea pig. As a general rule tissue taken from one animal will not grow in an animal of a different species. However, since the anterior chamber of the eye is one of the few parts of the body that does not possess this species immunity, it makes an ideal transplantation site. A small cut was made near the superior margin of the corneo-scleral junction and a small fragment of tumor tissue was forced into the inferior angle of the iris. Growth of the tumor tissue was indicated at the end of two weeks by a pink coloration, and vascularization was completed within 50 days. The tumors then began to regres but never completely disappeared and would grow again to refill the anterior chamber.

Before the development of this technique, it had been possible to transplant tumor tissue only to another member of the same species and this precluded the possibility of using human material. But with the perfection of this method these difficulties disappeared and another important step was taken towards the solution of the cancer problem.

Yolk Sac Cultivation

Since I have had personal experience with this method while working with Dr. Armstrong and Dr. Ham in the Department of Anatomy at Toronto, I shall describe it in somewhat greater detail. The procedure followed was very similar to that used by Taylor. The eggs were fertile and obtained from a flock of pure-

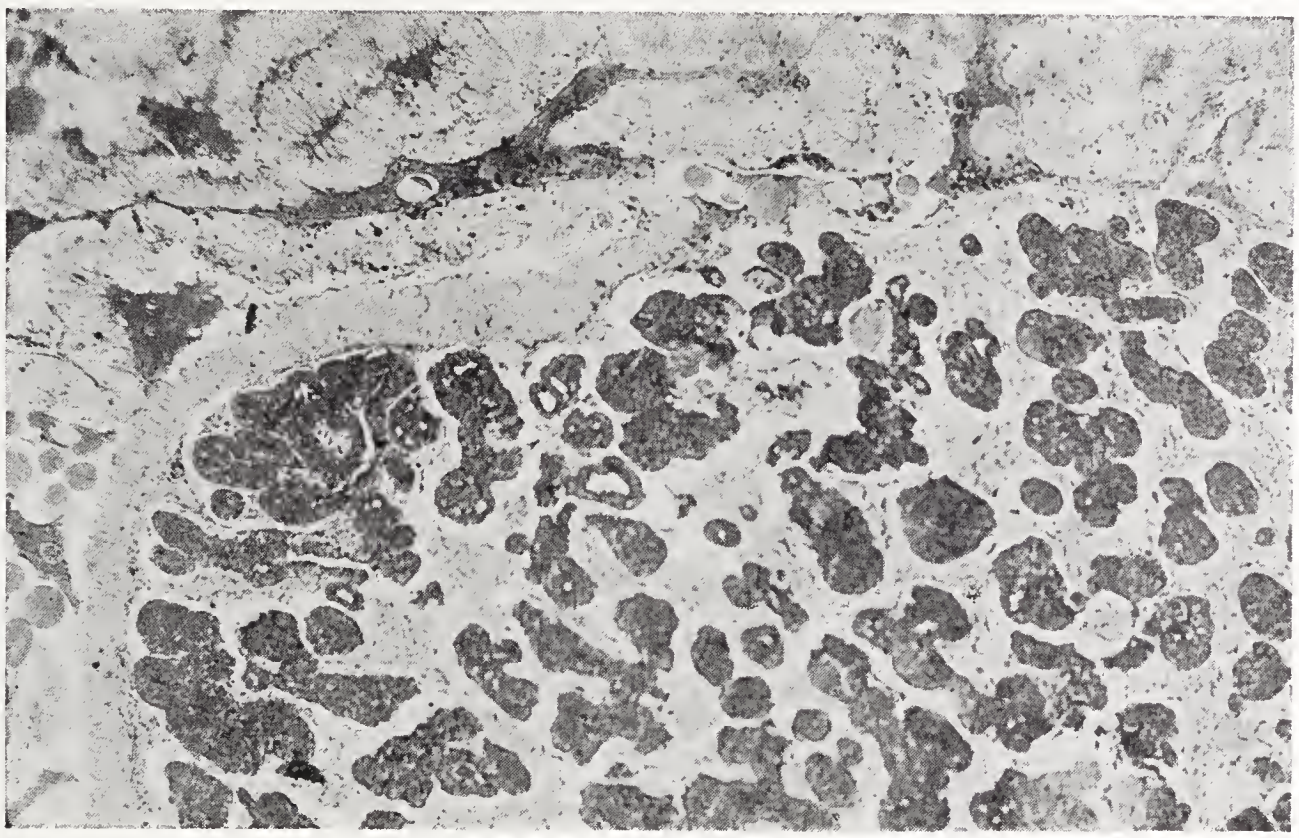

Fig. 2. *Section of mouse mammary tumor growing in the yolk sac of a developing chick embryo..* Note the clear margin of the youk sac separating the heavily staining clumps of tumor cells which are supported by mesodermal stroma from the homogeneous patches of yolk fluid in the yolk sac.

bred hens. They were incubated four days at 37.5°C. before injection. At the end of this time, they were placed on their sides in a sterile cabinet where the injection of tumor tissue was carried out. Aseptic technique was necessary throughout for the eggs possess no immunity until about the nineteenth day of development and for this reason fall easy prey to any invading organism. The eggs were placed on their sides, and since the embryo floats to the top of the yolk the syringe needle was inserted upwards at an angle of about 45° through a small hole in the shell over the air space and 0.5 cc. of diluted tumor tissue was injected into the yolk sac. (Fig. 1) The hole was then sealed with sterile wax and the eggs returned to the incubator.

Spontaneous mammary tumors were used for these experiments. The tissue was obtained either directly from the animal in which case it was diluted one in four with .85% sterile saline, or it was tumor tissue that had already grown for one or more generations in eggs and in this case was diluted one in four with yolk and other egg fluids before injection. In the first case where the tumor was taken directly from the animal it was difficult to initiate its growth in the eggs and many tumors were transplanted before one of them finally grew successfully. Once the growth was initiated in eggs, however, there was no difficulty in maintaining its serial transfer.

The removal of the tumor from the egg was also carried out under aseptic conditions. The shell was removed over the air space, the inner shell membrane taken away and the whole content of the shell emptied carefully into a sterile petri dish. The tumor, which grew at the advancing edge of the yolk sac, was thus adequately exposed and easily cut loose. The tissue which was obtained in this manner was diluted as explained above and injected into fresh eggs. Histologically, the transplanted tumors were found to be identical with the original mouse mammary tumors. (Fig. 2). When the tumor cells are injected into the egg, they become embedded in the mesoderm of the advancing edge of the yolk sac and fibrous tissue and vessels from this mesoderm grow among the cells and support and nourish them.

Obviously, the outstanding advantage in this method is that tumor tissue from other species can be grown in the yolk sac of the developing chick embryo because the chick does not develop any immunity until about the nineteenth day of incubation. Furthermore, if asepctic operational conditions are observed, the egg is free from complicating infections which are endemic in animals and this, combined with the speed of growth, the size the tumor attains and the lack of necrosis in the tumor, makes the yolk sac transplantation technique an exceptionally valuable one.

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Feature

C. L. RODGERS, Editor

MEDICAL ELECTIONS

A quarter of a century has passed since the first Meds Elections, and in the intervening period the Medical Elections have paralleled, in their own small way, the affairs of the world at large. During the first Great War the Elections waned somewhat, but in the roarng Twenties rose to boisterous heights, and the rowdy spirit of the era was clearly reflected in the affairs of the faculty. During the Thirties, times were more precarious, and although the students maintained an avid interest in their government, some of the gaudy showmanship was lost. When the second Great War struck, the student government became of small import to the average student, who, in the haste and pressure of a wartime education, had very little time for anything but consideration of himself, and the support and spirit upon which every election depends for success fell to a minimum.

But this year the Elections showed a pronounced trend for the better, and it looks as though some of the old spirit is returning. About 90% of the students have voted, a considerable increase over previous years, and thereby directly assured themselves of a more representative and energetic Society.

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Abstracts

C. L. ASZKANAZY, Editor

Contributors

C. L. Aszkanazy
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C. R. Johnson

MEDICINE I

Clinical Syndrome of Potassium Intoxication. C. A. Finch, C. G. Sawyer, J. M. Flynn: Amer. J. Med. *1,* 337-352 (1946)

Two cases of elevated serum potassium are described. The clinical syndrome of potassium intoxication is associated with a widespread impairment of neuromuscular function. There is a characteristic sequence of electrocardiographic changes, impaired contraction of the heart which may be readily recognized by ausculation, and final stopping of the heart in diastole. Flaccid paralysis of the extremities and to a lesser degree of the trunk may be present, however, the cranial nerves are usually not involved. Following the administration of sodium chloride both the electrocardiographic changes and the paralysis reverted toward normal. The authors point out that muscle contraction is interfered with by either a deficiency or excess of serum calcium and that the accumulation of potassium in the human body to a level of about 40 mg. per cent. is lethal owing to its effect on the myocardium.

W. G. B. C.

MEDICINE II

Hemolytic Streptococcic and Nonstreptococcic Diseases of the Respiratory Tract: Comparative Clinical Study. L. A. Rantz, P. J. Boisvert, and W. W. Spink: Arch. Internal Med. *78,* 369-386 (1946)

Rantz and his associates found that hemolytic streptococcic infections of the respiratory tract are usually acute in onset and usually associated with headache, chills, generalized aching and prostration. A sore throat with tonsillar and pharyngeal exudate and redness and edema of the pharyngeal tissues are the prevailing symptoms. Tender anterior cervical glands are frequently observed. A cough and hoarseness are the typical features of nonstreptococcic infections of the respiratory tract. Nasopharyngeal tissues are nearly normal. There is a minimum or no exudate, edema, and redness. Rarely are there any tender anterior cervical glands. The authors estimate that an accuracy of 70% may be expected in differentiating between streptococcic and nonstreptococcic disease of the respiratory tract in adults in the northern United States may be expected on the basis of the findings, and upon the inclusion of a bacteriologic study of the throat flora an accuracy of 80-90% may be expected. Differential diagnosis in the southern states would be more difficult owing to the lower incidence of streptococcic infections and the prevalence of atypical nonstreptococcic diseases.

W. G. B. C.

MEDICINE III

Klatskin G. and Rappaport E. M. "Late Residuals in Presumably Cured Acute Infectious Hepatitis" Annals Int. Med. 26:13 Jan. 1947.

217 patients with a clearcut history of hepatitis were reviewed after an interval of 2 months to 27 years after the disease. A careful history was taken in each case, an abdominal examination done and liver function tests performed. The latter were tests for serum bilirubin, Maclachlan thymol turbidity, cephalin cholesterol flucculation and brom-sulphalein excretion.

22% had symptoms referrable to the liver, chiefly fat intolerance, liver tenderness or epigastric or right upper quadrant pain; 27% showed hepatomegaly; and 19% had evidence of impaired liver function, as determined by the above mentioned tests. 50% of all the patients reviewed had one or more of the above signs and symptoms.

The only factor showing relation to the occurrence of residuals was the duration and severity of jaundice. The type of hepatitis, age of the patient, alcohol consumption, malnutrition, recurrences, and syphilis apparently have no influence on the occurrence of residual liver damage.

C. L. A.

SURGERY I

Merle Scott W. J. and Serenatii I. J. "Megacolon, Mechanism and Choice of Treatment" Surgery *20* (5) : 603 Nov. 1946.

The authors classify the syndrome under 4 etiological mechanisms:

(1) Organic obstruction of congenital origin—This is associated with anomalous development or fusion of the proctodeum which causes a certain amount of obstruction to the lower large bowel. Antiobstipation management with gradual dilatation is successful in this type of megacolon.

(2) Neurogenic dysfunction—In such cases, spinal anaesthesia produces indirectly marked evacuation of the bowel. If this does not result in lasting improvement, lumbar sympathectomy is to be considered.

(3) Functional obstruction (Doilichocolon)—Here an abnormally long sigmoid causes kinking. Treatment consists of resection of the redundant bowel, using a wide side to side anastomosis instead of the Mikulicz type of resection.

(4) Extrinsic metabolic effects—A few cases have been related to metabolic disturbances, e.g. avitaminosis, malnutrition, thyroid deficiency, but it is not definite that such conditions are clinical entities.

A plan of management of all cases is outlined:

(a) Determination whether the megacolon is due to organic obstruction of congenital origin or due to metabolic disturbances.

(b) Medical treatment for all idiopathic cases consists of colonic irrigation, mild catharsis and parasympathetic drugs.

(c) Surgical treatment consists of resection of the bowel, where indicated, or sympathectomy after successful spinal anaesthesia.

C. R. J.

SURGERY II

Baritell A. L. "Perforated Duodenal Ulcer" Surgery *21* (*1*) : 24 Jan. 1947.

Improper treatment of this emergency has caused a mortality of 10—25%. A series of 88 unpicked cases is discussed, treated by operation with a mortality of 1.1%.

Men are affected more often than women, at a ratio of 3:1. 57 cases had a previous ulcer history. The age incidence was chiefly between 30 and 50 years. Complications were rare, being chiefly wound infection and subphrenic abscess. The average post-operative hospital stay was 14.3 days. Of 9 un-operated cases, 2 died.

An outline of the operative treatment is presented:

(1) Rapid pre-operative physical examination, diagnosis, and preparation for operation.
(2) Spinal anaesthesia.
(3) At operation an omental patch is applied to the perforation by a few interrupted cotton sutures, without attempt at closure of the perforation. This is of special value, where oedema and induration surround the perforation.
(4) Post-operatively, glucose in saline, 1/6 molar sodium lactatesulphadiazine are given intravenously and suction applied to the stomach for 48 hours.

C. R. J.

SURGERY III

Clinical Manifestations of Local Shock and Treatment. J. E. M. Thompson: Surgery, *20,* 498-510 (1946)

Thompson regards local shock as a clinical sequence of pathological changes exhibited after severe injuries, especially crushing, of the extremities, characterized by local vasospasm. Initially it acts as a safety measure to stop hemorrhage and additional trauma. Later, capillary dilatation, incompetence or decompensation may result with consequent prevention of normal tissue metabolism, interference with normal interchange of tissue fluids in the injured region with loss of plasma, accumulation of the products of the trauma, and often degeneration of tissues and necrosis.

As a result of studies on more than three hundred rabbits the author concludes that procaine block of the sympathetics controlling a severely injured extremity tends to restore circulatory integrity and equilibrium. Capillary competence, tissue fluid interchange, organization of clots, the appearance of fibroblasts, proliferation of capillaries, calcification of necrotic muscle tissue, and early healing were all found to be stimulated by thus arresting vasoconstriction. The author does almost routinely a procaine sympathetic block on all cases with severe injuries to the extremities. He presents four striking examples from a series of forty-eight cases in which he has employed either stellate or lumbar sympathetic block.

SURGERY IV

CASE OF ADDISON'S DISEASE SUCCESSFULLY TREATED BY GRAFT. L. R. Broster and H. Gardiner-Hill: British Med. J. *2*, 570-572 (1946)

The case is presented of a young woman in whom, nine months previous to the authors' seeing her, a diagnosis of Addison's disease was made. This diagnosis was confirmed by the authors. An adrenal gland from a patient with the adrenogenital syndrome (hyperplasia) was ingrafted. As a result, the woman lost her signs and symptoms of Addison's disease and her blood sodium level was found to no longer fall below normal. The most recent sodium chloride withdrawal test reported (14 months after the ingrafting) showed that this change had been maintained.

W. G. B. C.

PUBLIC HEALTH I

TUBERCULOSIS AS AN OCCUPATIONAL HAZARD DURING MEDICAL TRAINING: REPORT OF CASE FINDING AND FOLLOW-UP STUDY, WITH AN EFFECTIVE CONTROL PROGRAMME FOR TUBERCULOSIS IN WOMEN MEDICAL STUDENTS. Sarah I. Morris: Amer. Rev. Tuberculosis *54*, 159-165 (1946)

Intimate exposure to tuberculous patients and materials, at the most vulnerable age, represents a potential hazard for medical students. The influence of sex on the incidence of tuberculosis is still controversial, but data at present available suggest an earlier onset and an earlier peak mortality in women than in men. Because the duties and average ages are not comparable, the comparison of male medical students with nursing students is misleading and consequently Morris has reported the findings at the women's medical school during the development of a programme for studying tuberculosis in women medical students. The period from 1932 to 1944 is surveyed. During this time 449 students were observed and 56 cases of tuberculosis were analysed. The disease was found to occur earlier and to progress more rapidly in women than in men. The chief sources of infection were necropsy service and the use of tuberculous patients for demonstrations in physical diagnosis and for clinical training.

When the withdrawal of an infected student is delayed, or a student returns before complete stabilization, relapse and transmission of the infection to others may be expected. It is imperative that there be an adequate control programme in medical schools and hospitals. It should include efficient case-finding and follow-up programmes in medical schools and the establishment of safer techniques in necropsy rooms, laboratories, clinics and hospital wards. Entrance and periodic examinations of internes and residents, routine examinations of all college and hospital personnel, including ambulatory and bed patients, and early care of all tuberculous patients should be obligatory.

W. G. B. C.

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[1]The evaluation of Preparations of the vitamin B-Complex. C.M.A.J. May, 1942.

[2]Council on Pharmacy and Chemistry and Council on Foods and Nutrition. J.A.M.A. 119-12-948.

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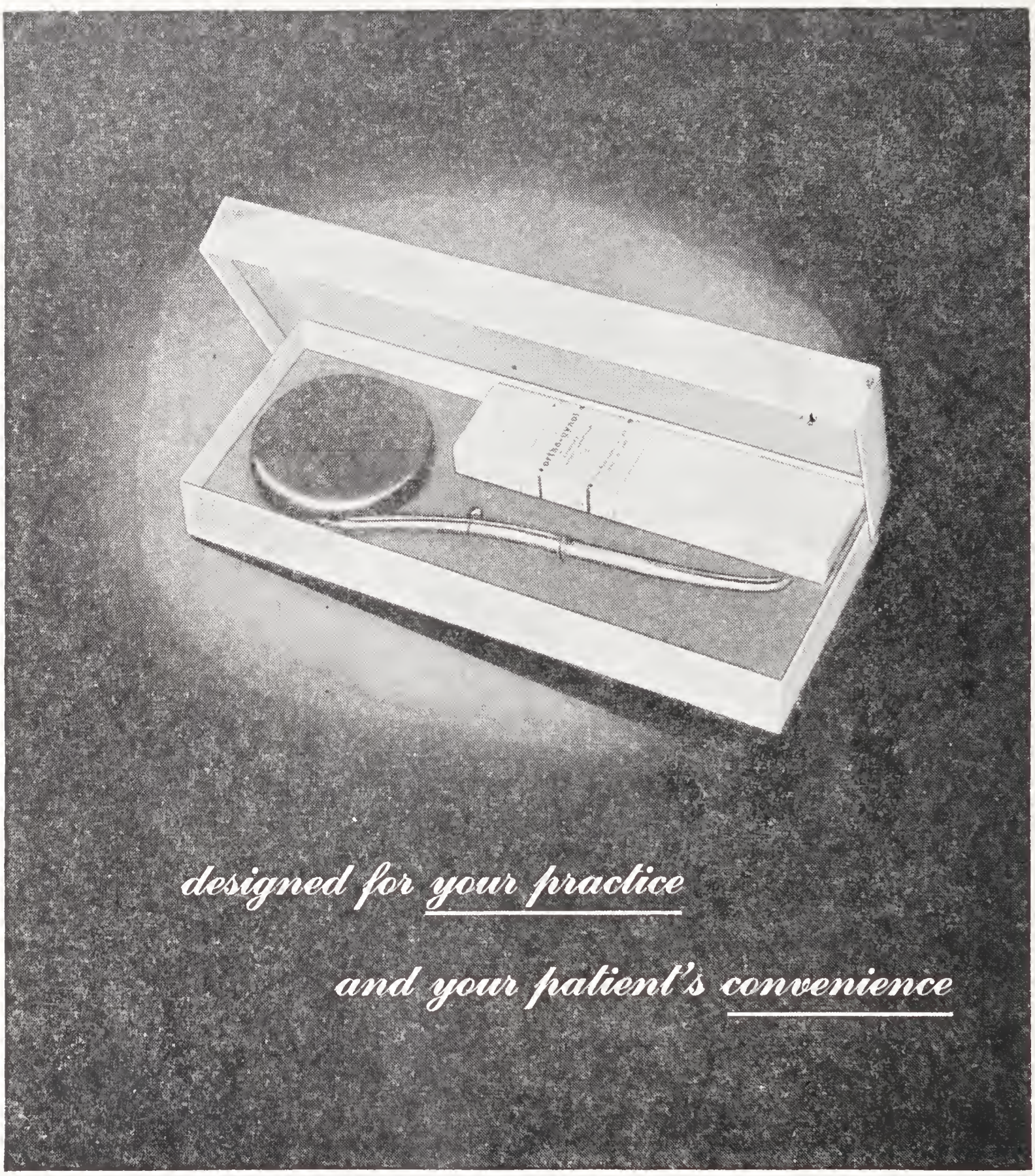

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